REMARKS

The Amendment, filed in response to the Office Action of February 28, 2011 is believed to fully address all issues contained in the Office Action. Favorable reconsideration and allowance of the application are respectfully requested.

Disposition of Claims and Claim Amendment

As of the mailing date of the Office Action, claims 1-13 and 16 have been pending in the application, of which claims 8-12 have been withdrawn from consideration as being directed to non-elected subject matter.

In the current Amendment, claim 1 is amended to remove parenthesis expressions. Claim 16 is amended to correct a typographical error and to more clearly set forth the claimed subject matter.

No new matter is introduced. Entry and consideration of the amendment are respectfully requested.

Withdrawn Rejections

Applicant thank the Examiner for withdrawing the previous rejections in view of Applicant's amendments and/or arguments.

Applicant also thank the Examiner for acknowledging and entering the computer readable form of the sequence listing.

Response to Objection to the Claims

The Examiner has objected to claim 16 for an alleged informality. In particular, the Examiner identified a typographical error in line 3 of the claim.

The Object is rendered moot in light of the amendment made to claim 16 as discussed above.

Withdrawal of the objection is respectfully requested.

Currently Amended Claim 16 Meets Written Description Requirement

Claim 16 has rejected as allegedly encompassing subject matter that is not supported by the original disclosure or claims as filed.

Without conceding the rejection, solely for interests of Applicant to advance the prosecution, Applicant amends claim 16 to recite "3.4 kDa or 10 kDa," rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

Claims 1-7, 13 and 16 are Patentable Under 35 U.S.C. § 103

In the Office Action, Claims 1-7, 13, and 16 are rejected as assertedly being unpatentable over Kostenuik *et al.* (U.S. Pat. No. 6,756,480; hereinafter, "Kostenuik") in view of Bentz (*J. Biomed. Mat. Res.*, 36(4):539-548, 1998, hereinafter, "Bentz") and Mohamed *et al.* (U.S. Pub. No. 2006/0153839; hereinafter, "Mohamed").

According to the Examiner, Kostenuik teaches parathyroid hormone peptide (PHP) covalently linked to an Fc domain via a linker that can be PEG. However, the Examiner acknowledges that Kostenuik does not exemplify Fc-nonpeptide linker-PHP.

The Examiner relies upon the disclosure of Bentz to support the assertion that methods of covalently linking proteins with non-peptide linkers such as polyethylene glycol were well known in the art at the time the invention was made. In addition, Mohamed is cited for allegedly

teaching methods of producing bispecific proteins molecules using PEG linkers having formula of X-PEG-Y.

Applicant respectfully, but strongly disagrees for the following reasons.

Kostenuik only discloses PTH-Fc and PTHrP-Fc conjugates prepared as fusion proteins by a recombinant method, but there is no disclosure in its examples concerning the non-fusion conjugate comprised of PTH, non-peptide linker, and Fc wherein the Fc fragment is covalently linked to the drug, as recited in claims of the instant application.

Specifically, Kostenuik teaches a peptide molecule-excipient conjugate wherein the peptide molecule can be a PTH/PTHrP control domain sequence, and the excipient can be an Fc domain or PEG. That is, the conjugate derived from Kostenuik is in the form of PTH/PTHrP-Fc or PTH/PTHrP-PEG. In addition, as referring to the detailed description of Kostenuik, the case wherein an excipient is an Fc domain, the Fc domain is fused to the C-terminus of a peptide molecule.

In this juncture, in Kostenuik, when the excipient is an Fc domain, only a peptide linker will be used in the preparation of a conjugate because the conjugate needs to be prepared by a recombinant method in the form of a fusion protein. In such a case, it is only possible to prepare PTH/PTHrP-Fc conjugates or PTH/PTIIrP-peptide linker-Fc conjugates.

In contrast, in Kostenuik, when the excipient is PEG, a peptide molecule and PEG are covalently linked via a chemical linkage, using a non-peptide linker such as PEG. In such a cuse, it is only possible to prepare PT-HIPTHrP-PEG conjugates or-PT-HIPTHrP-PEG-PEG conjugates as a non-fusion conjugate.

That is, the use of PEG as a non-peptide linker in Kostenuik can be applied only in using a polymer excipient such as PEG, and a non-peptide linker cannot be used when using an Fc domain which is fused to the C-terminus of a peptide molecule as an excipient.

In addition, Kostenutk discloses the use of PEG having a molecular weight of 100 kDa-5,000 kDa or preferably 100 kDa-500 kDa as a non-peptide linker, whereas the subject matter of claim 16 uses a PEG having a molecular weight of 3.4 kDa or 10 kDa. Further, according to the examples, as the molecular weight of PEG increases, the serum half life of a protein conjugate is reduced (Examples 2-4). In this light, the molecular weight of PEG disclosed in Kostenuik is not only different than that of the present invention, but it can also result in the reduction of serum half life of the target protein which can be significantly reduced in the case of preparing a protein conjugate using the PEG disclosed in Kostenuik.

In conclusion, Kostenuik does not disclose the limitation of the claims that requires an IgG Fc fragment and a physiologically active polypeptide are covalently linked via a non-peptide linker as a drug carrier, not fused by a recombinant method. Therefore, it is not possible to derive the non-fusion conjugate prepared using a non-peptide linker from the technical concept of Kostenuik, nor can a fusion protein be prepared using a non-peptide linker.

Further, Bentz merely discloses that PEG is a biocompatible hydrophilic polymer that has been successfully used in modifying a peptide growth factor such as TGF-β2, and Mohamed only discloses a method for preparing bispecific proteins using PEG linkers. As such, even if assuming *arguendo* Kostenuik, Bentz and Mohamed maybe combined, which Applicant does not agree, the combined teaching does not disclose each and every limitation of claims 1 and 16, and dependent claims 2-7 and 13. And, nowhere in Kostenuik, Bentz and Mohamed is guidance or

teaching to modify their defective teaching to reach the claimed subject matter with reasonable expectation of success.

Response to Obviousness-Type Double Patenting Rejections

The Examiner maintains the provisional rejection of claims 1-7, 13, and 16 as allegedly being unpatentable over claims 1-25 of co-pending U.S. Serial No. 11/910,962 for reasons of record. According to the Examiner, the argument set forth in the previous response was not persuasive because the Examiner has maintained the above-discussed rejections.

With regard to copending USSN 11/910,962, Applicant respectfully submits that this copending application has a later filing date (April 28, 2005) than the filing date of the instant application (October 13, 2004, which is the PCT filing date), and the claims of the instant application are otherwise in condition for allowance as discussed above, the provisional rejection cannot be sustained. MPEP 804 ("If "provisional" ODP rejections in two applications are the only rejections remaining in those applications, the examiner should withdraw the ODP rejection in the earlier filed application thereby permitting that application to issue without need of a terminal disclaimer.").

Alternatively, Applicant again respectfully request the provisional rejection be held in abeyance until the claims are in condition for allowance.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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